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DATE: Monday, November 08, 2004

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	DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=AND		
☐	L1	dam.clm.	3925
☐	L2	L1 and salmonel$.clm.	12

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First Hit Fwd Refs

L2: Entry 11 of 12 File: USPT May 7, 2002

DOCUMENT-IDENTIFIER: US 6383496 B1
TITLE: Recombinant vaccines comprising immunogenic attenuated bacteria having RPOS positive phenotype

CLAIMS:

3. The method according to claim 1 wherein the bacteria is a strain of Salmonella.

4. The method according to claim 3 wherein the Salmonella is a strain of S. typhi.

5. The method according to claim 4 wherein the one or more inactivating mutations are in a gene selected from the group consisting of a pab gene, a pur gene, an aro gene, asd, a dap gene, nadA, pncB, galE, pmi, fur, rpsL, ompR, htrA, hemA, cdt, cya, crp, dam, phoP, phoQ, rfc, poxA, galU, metL, metH, mviA, sodC, recA, ssrA, ssrB, sirA, sirB, sirC, inv, hilA, hilC, hilD, rpoE, flgM, tonB, and slyA.

10. A carrier bacteria according to claim 8 wherein the bacteria is a Salmonella.

11. A carrier bacteria according to claim 10 wherein the Salmonella is an S. typhi.

12. The carrier bacteria according to claim 11 wherein the one or more inactivating mutations are in a gene selected from the group consisting of a pab gene, a pur gene, an aro gene, asd, a dap gene, nadA, pncB, galE, pmi, fur, rpsL, ompR, htrA, hemA, cdt, cya, crp, dam, phoP, phoQ, rfc, poxA, galU, metL, metH, mviA, sodC, recA, recA, ssrA, ssrB, sirA, sirB, sirC, inv, hilA, hilC, hilD, rpoE, flgM, tonB, and slyA.

17. The composition according to claim 15 wherein the bacteria is a Salmonella.

18. The composition according to claim 17 whreein the Salmonella is an S. typhi.

19. The composition according to claim 18 wherein the one or more inactivating mutations are in a gene selected from the group consisting of a pab gene, a pur gene, an aro gene, asd, a dap gene, nadA, pncB, galE, pmi, fur, rpsL, ompR, htrA, hemA, cdt, cya, crp, dam, phoP, phoQ, rfc, poxA, galU, metL, metH, mviA, sodC, recA, recA, ssrA, ssrB, sirA, sirB, sirC, inv, hilA, hilC, hilD, rpoE, flgM, tonB,and slyA.

25. The genetically engineered bacterial cell according to claim 23 wherein the strain of bacteria is a strain of Salmonella.

26. The genetically engineered bacterial cell according to claim 25 wherein the strain of Salmonella is a strain of S. typhi.

27. The genetically engineered bacterial cell according to claim 26 wherein the one or more inactivating mutations are in a gene selected from the group consisting of a pab gene, a pur gene, an aro gene, asd, a dap gene, nadA, pncB, galE, pmi, fur, rpsL, ompR, htrA, hemA, cdt, cya, crp, dam, phoP, phoQ, rfc, poxA, galU, metL, metH, metH, mviA, sodC, recA, ssrA, ssrB, sirA, sirB, sirC, inv, hilA, hilC, hilD, rpoE, flgM, tonB, and slyA.

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SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R) 1951-2004/Oct W5
         (c) format only 2004 The Dialog Corp.
*File 155: Medline will stop updating COMPLETED records on November 17,
2004. Please see HELP NEWS 155 for details.
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         2001 (c) Action Potential
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  File  98:General Sci Abs/Full-Text 1984-2004/Sep
         (c) 2004 The HW Wilson Co.
  File 135:NewsRx Weekly Reports 1995-2004/Oct W5
         (c) 2004 NewsRx
*File 135: New newsletters are now added. See Help News135 for the
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  File 144:Pascal 1973-2004/Oct W5
         (c) 2004 INIST/CNRS
  File 149:TGG Health&Wellness DB(SM) 1976-2004/Oct W3
         (c) 2004 The Gale Group
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         (c) format only 2004 The Dialog Corporation
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  File 159:Cancerlit 1975-2002/Oct
         (c) format only 2002 Dialog Corporation
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Please see HELP NEWS159.
  File 162:Global Health 1983-2004/Sep
         (c) 2004 CAB International
  File 164:Allied & Complementary Medicine 1984-2004/Nov
         (c) 2004 BLHCIS
  File 172:EMBASE Alert 2004/Oct W5
         (c) 2004 Elsevier Science B.V.
  File 266:FEDRIP 2004/Aug
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  File 369:New Scientist 1994-2004/Oct W4
         (c) 2004 Reed Business Information Ltd.
  File 370:Science 1996-1999/Jul W3
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information.
  File 399:CA SEARCH(R) 1967-2004/UD=14120
         (c) 2004 American Chemical Society
*File 399: Use is subject to the terms of your user/customer agreement.
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  File 444:New England Journal of Med. 1985-2004/Oct W5
         (c) 2004 Mass. Med. Soc.
  File 467:ExtraMED(tm) 2000/Dec
         (c) 2001 Informania Ltd.
*File 467: F467 no longer updates; see Help News467.
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      Set  Items  Description
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Set     Items   Description
S1        732   DNA?/TI AND ADENINE?/TI AND (METHYLASE? OR METHYLTRANSFERA-
            SE?)/TI
S2        296   S1/2000:2004
S3        436   S1 NOT S2
S4        172   RD (unique items)
S5        144   S3 AND (ATTENUAT? OR MUTANT? OR INSERT? OR DELET? OR TRANS-
            POS?)
S6         92   S5 AND (SALMON? OR COLI OR VIBRIO? OR PASTEUR? OR SHIGEL? -
            OR NEISSERI?)
?t s6/9/1-14

 6/9/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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14504804   PMID: 10500219
    DNA adenine methylase mutants of Salmonella typhimurium show
defects in protein secretion, cell invasion, and M cell cytotoxicity.
  Garcia-Del Portillo F; Pucciarelli M G; Casadesus J
  Centro de Biologia Molecular "Severo Ochoa," Universidad Autonoma de
Madrid-Consejo Superior de Investigaciones Cientificas, Cantoblanco, Madrid
28049, Spain.
  Proceedings of the National Academy of Sciences of the United States of
America (UNITED STATES) Sep 28 1999, 96 (20) p11578-83, ISSN
0027-8424 Journal Code: 7505876
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: Completed
  Subfile: INDEX MEDICUS
    Mutants of Salmonella typhimurium lacking DNA adenine methylase are
 attenuated for virulence in BALB/c mice. LD(50) values of a DNA adenine
methylation (Dam)(-) mutant are at least 10(3)- to 10(4)-fold higher than
those of the parental strain when administrated by oral or intraperitoneal
routes. Dam(-) mutants are unable to proliferate in target organs but
persist in low numbers in these locations. Efficient protection to
challenge with the virulent parental strain is observed in mice infected
with a Dam(-) mutant . Use of the ileal loop assay shows that Dam(-)
 mutants are less cytotoxic to M cells and fail to invade enterocytes. In
the tissue culture model, lack of DNA adenine methylation causes reduced
ability to invade nonphagocytic cells. In contrast, no effect is observed
either in intracellular proliferation within nonphagocytic cells or in
survival within macrophages. The invasion defect of Dam(-) mutants is
correlated with a distinct pattern of secreted proteins, which is observed
in both PhoP(+) and PhoP(-) backgrounds. Altogether, our observations
suggest a multifactorial role of Dam methylation in Salmonella virulence.
  Tags: Female; Human; Support, Non-U.S. Gov't
  Descriptors: Bacterial Proteins--secretion--SE; *Intestinal Mucosa
--microbiology--MI; * Salmonella typhimurium--enzymology--EN;
*Site-Specific DNA-Methyltransferase (Adenine-Specific)--physiology--PH;
Animals; DNA Methylation; Hela Cells; Mice; Mice, Inbred BALB C; Mutation;
 Salmonella typhimurium--metabolism--ME; Salmonella typhimurium
--pathogenicity--PY; Site-Specific DNA-Methyltransferase (Adenine-Specific)
--genetics--GE; Virulence
  CAS Registry No.: 0 (Bacterial Proteins)
  Enzyme No.: EC 2.1.1.72 (Site-Specific DNA-Methyltransferase
(Adenine-Specific))
  Record Date Created: 19991021
  Record Date Completed: 19991021
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6/9/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13880569 PMID: 9575240
A temperature-sensitive DNA adenine methyltransferase mutant **of** Salmonella **typhimurium.**
Brawer R; Batista F D; Burrone O R; Sordelli D O; Cerquetti M C
Centro de Estudios Farmacoligicos y Botanicos (CEFYBO-CONICET) and University of Buenos Aires, School of Medicine, Serrano 669, 1414 Buenos Aires, Argentina.
Archives of microbiology (GERMANY) Jun 1998, 169 (6) p530-3, ISSN 0302-8933 Journal Code: 0410427
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
A temperature-sensitive **mutant** of **Salmonella** typhimurium was isolated earlier after **transposon** mutagenesis with Tn10d Tet. The **mutant** D220 grows well at 28 degreesC but has a lower growth rate and forms filaments at 37 degreesC. **Transposon** -flanking fragments of **mutant** D220 DNA were cloned and sequenced. The **transposon** was **inserted** in the dam gene between positions 803 and 804 (assigned allele number: dam-231 : : Tn10d Tet) and resulted in a predicted ten-amino-acid-shorter Dam protein. The **insertion** created a stop codon that led to a truncated Dam protein with a temperature-sensitive phenotype. The **insertion** dam-231 : : Tn10d Tet resulted in a dam "leaky" phenotype since methylated and unmethylated adenines in GATC sequences were present. In addition, the dam-231 : : Tn10d Tet **insertion** rendered dam **mutants** temperature-sensitive for growth depending upon the genetic background of the S. typhimurium strain. The wild-type dam gene of S. typhimurium exhibited 82% identity with the Escherichia **coli** dam gene.
Tags: Support, Non-U.S. Gov't
Descriptors: **Salmonella** typhimurium--enzymology--EN; *Site-Specific DNA-Methyltransferase (Adenine-Specific)--genetics--GE; DNA **Transposable** Elements--genetics--GE; Polymerase Chain Reaction; **Salmonella** typhimurium--genetics--GE; **Salmonella** typhimurium --growth and development--GD; Site-Specific DNA-Methyltransferase (Adenine-Specific) --isolation and purification--IP; Temperature
CAS Registry No.: 0 . (DNA Transposable Elements)
Enzyme No.: EC 2.1.1.- (Dam methyltransferase); EC 2.1.1.72 (Site-Specific DNA-Methyltransferase (Adenine-Specific))
Record Date Created: 19980713
Record Date Completed: 19980713

6/9/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

13209695 PMID: 8878670
DNA adenine methylase mutants **of** Salmonella **typhimurium and a novel dam-regulated locus.**
Torreblanca J; Casadesus J
Departamento de Genetica, Facultad de Biologia, Universidad de Sevilla, Spain.
Genetics (UNITED STATES) Sep 1996, 144 (1) p15-26, ISSN 0016-6731 Journal Code: 0374636
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Mutants of **Salmonella** typhimurium lacking DNA adenine methylase were isolated; they include **insertion** and **deletion** alleles. The dam locus maps at 75 min between cysG and aroB, similar to the Escherichia **coli** dam

gene. Dam- **mutants** of S. typhimurium resemble those of E **coli** in the following phenotypes: (1) increased spontaneous mutations, (2) moderate SOS induction, (3) enhancement of duplication segregation, (4) inviability of dam recA and dam recB **mutants** , and (5) suppression of the inviability of the dam recA and dam recB combinations by mutations that eliminate mismatch repair. However, differences between S. typhimurium and E. **coli** dam **mutants** are also found: (1) S. typhimurium dam **mutants** do not show increased UV sensitivity, suggesting that methyl-directed mismatch repair does not participate in the repair of UV-induced DNA damage in **Salmonella** . (2) S. typhimurium dam recJ **mutants** are viable, suggesting that the **Salmonella** RecJ function does not participate in the repair of DNA strand breaks formed in the absence of Dam methylation. We also describe a genetic screen for detecting novel genes regulated by Dam methylation and a locus repressed by Dam methylation in the S. typhimurium virulence (or "cryptic") plasmid.

Tags: Support, Non-U.S. Gov't

Descriptors: **Salmonella** typhimurium--enzymology--EN; *Site-Specific DNA-Methyltransferase (Adenine-Specific)--genetics--GE; Chromosome Mapping; Cloning, Molecular; DNA Methylation; DNA **Transposable** Elements; Gene **Deletion** ; Genetic Complementation Test; Mutagenesis, **Insertional** ; **Salmonella** typhimurium--genetics--GE; **Salmonella** typhimurium --radiation effects--RE; Site-Specific DNA-Methyltransferase (Adenine-Specific)--metabolism--ME; Ultraviolet Rays

CAS Registry No.: 0 (DNA Transposable Elements)

Enzyme No.: EC 2.1.1.- (Dam methyltransferase); EC 2.1.1.72 (Site-Specific DNA-Methyltransferase (Adenine-Specific))

Record Date Created: 19970128

Record Date Completed: 19970128

6/9/4 (Item 4 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

10004952 PMID: 8125341

The DNA adenine methyltransferase **-encoding gene (dam) of** Vibrio **cholerae.**

Bandyopadhyay R; Das J

Biophysics Division, Indian Institute of Chemical Biology, Calcutta.

Gene (NETHERLANDS) Mar 11 1994, 140 (1) p67-71, ISSN 0378-1119 Journal Code: 7706761

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

The DNA adenine methyltransferase (MTase)-encoding gene (dam) of **Vibrio** cholerae, an organism belonging to the family **Vibrionaceae** , has been cloned and the complete nucleotide (nt) sequence determined. V. cholerae dam encodes a 21.5-kDa protein and is directly involved in methyl-directed DNA mismatch repair. It can substitute for the Escherichia **coli** enzyme and can suppress the phenotypic traits associated with E. **coli** dam **mutants** . Overproduction of V. cholerae Dam MTase does not result in hypermutability in either V. cholerae or E. **coli** cells. Overproduction of V. cholerae Dam in a pUC plasmid, however, fails to suppress the 2-aminopurine (2-AP)-sensitive phenotype of E. **coli** dam **mutants** . Homology between the nt and deduced amino acid (aa) sequences of the E. **coli** and V. cholerae dam genes is only 30-35%.

Tags: Support, Non-U.S. Gov't

Descriptors: Methyltransferases--genetics--GE; *Site-Specific DNA-Methyltransferase (Adenine-Specific); * **Vibrio** cholerae--genetics--GE; Amino Acid Sequence; Base Sequence; Cloning, Molecular; DNA, Bacterial; Escherichia **coli** ; Genetic Complementation Test; Genetic Vectors; Molecular Sequence Data; Recombinant Proteins--genetics--GE; **Vibrio** cholerae--enzymology--EN

Molecular Sequence Databank No.: GENBANK/X67820

CAS Registry No.: 0 (DNA, Bacterial); 0 (Genetic Vectors); 0 (Recombinant Proteins)

Enzyme No.: EC 2.1.1. (Methyltransferases); EC 2.1.1.- (Dam methyltransferase); EC 2.1.1.72 (Site-Specific DNA-Methyltransferase (Adenine-Specific))
Gene Symbol: dam
Record Date Created: 19940414
Record Date Completed: 19940414

6/9/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09876948 PMID: 8226701
Analysis of the genetic requirements for viability of Escherichia coli **K-12** DNA adenine methylase **(dam)** mutants .
Peterson K R; Mount D W
Department of Molecular and Cellular Biology, University of Arizona, Tucson 85721.
Journal of bacteriology (UNITED STATES) Nov 1993, 175 (22) p7505-8, ISSN 0021-9193 Journal Code: 2985120R
Contract/Grant No.: GM24496; GM; NIGMS
Erratum in J Bacteriol 1994 Mar;176(5) 1554
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
RecBCD protein, necessary for Escherichia **coli** dam **mutant** viability, is directly required for DNA repair. Recombination genes recF+, recN+, recO+, and recQ+ are not essential for dam **mutant** viability; they are required for recBC sbcBC dam **mutant** survival. mutH, mutL, or mutS mutations do not suppress subinduction of SOS genes in dam **mutants** .
Tags: Support, U.S. Gov't, P.H.S.
Descriptors: Escherichia **coli** --enzymology--EN; *Escherichia **coli** --genetics--GE; *Methyltransferases--genetics--GE; *Site-Specific DNA-Methyltransferase (Adenine-Specific); Alleles; Exodeoxyribonuclease V; Exodeoxyribonucleases--genetics--GE; Exodeoxyribonucleases--metabolism--ME; Genes, Bacterial; Genotype; Methyltransferases--metabolism--ME; Rec A Recombinases--genetics--GE; Rec A Recombinases--metabolism--ME; Recombination, Genetic; SOS Response (Genetics); Suppression, Genetic
Enzyme No.: EC 2.1.1. (Methyltransferases); EC 2.1.1.- (Dam methyltransferase); EC 2.1.1.72 (Site-Specific DNA-Methyltransferase (Adenine-Specific)); EC 2.7.7.- (Rec A Recombinases); EC 3.1.- (Exodeoxyribonucleases); EC 3.1.11.5 (Exodeoxyribonuclease V); EC 3.1.11.5 (exodeoxyribonuclease V, E **coli**)
Gene Symbol: dam; lexA; recA; recB; recC; recF; recH; recN; recO; recQ; ryv; sulA
Record Date Created: 19931214
Record Date Completed: 19931214

6/9/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08550756 PMID: 2190555
Influence of DNA adenine methylase **on the sensitivity of Escherichia** coli **to near-ultraviolet radiation and hydrogen peroxide.**
Yallaly P; Eisenstark A
Division of Biological Sciences, University of Missouri, Columbia 65211.
Biochemical and biophysical research communications (UNITED STATES) May 31 1990, 169 (1) p64-9, ISSN 0006-291X Journal Code: 0372516
Contract/Grant No.: ES04489; ES; NIEHS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Subfile: INDEX MEDICUS
Near-ultraviolet (NUV) radiation and hydrogen peroxide (H2O2) inactivation studies were performed on Escherichia **coli** K-12 DNA adenine methylation (dam) **mutants** and on cells that carry plasmids which overexpress Dam methylase. Lack of methylation resulted in increased sensitivity to NUV and H2O2 (a photoproduct of NUV). In a dam **mutant** carrying a dam plasmid, the levels of Dam enzyme and resistance to NUV and H2O2 were restored. However, using a multicopy dam+ plasmid strain, increasing the methylase above wildtype levels resulted in an increase in sensitivity of the cells rather than resistance.
Tags: Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
Descriptors: Escherichia **coli** --enzymology--EN; *Hydrogen Peroxide --toxicity--TO; *Site-Specific DNA-Methyltransferase (Adenine-Specific) --physiology--PH; *Ultraviolet Rays--adverse effects--AE; Escherichia **coli** --drug effects--DE; Escherichia **coli** --radiation effects--RE; Plasmids
CAS Registry No.: 0 (Plasmids); 7722-84-1 (Hydrogen Peroxide)
Enzyme No.: EC 2.1.1.72 (Site-Specific DNA-Methyltransferase (Adenine-Specific))
Record Date Created: 19900711
Record Date Completed: 19900711

6/9/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08513379 PMID: 2185235
The DNA adenine methyltransferase **(dam+) gene of bacteriophage T4 reverses the mutator phenotype of an Escherichia** coli **dam** mutant .
Hall R M
Laboratory for Molecular Biology, CSIRO Division of Biotechnology, North Ryde, NSW, Australia.
Journal of bacteriology (UNITED STATES) May 1990, 172 (5) p2812-3, ISSN 0021-9193 Journal Code: 2985120R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
The mutator phenotype of Escherichia **coli** dam **mutants** was found to be reversed by introduction of the bacteriophage T4 gene for DNA adenine methyltransferase. This precludes a direct role for the E. **coli** DNA adenine methyltransferase in mismatch repair, in addition to its role in strand discrimination, as suggested by earlier studies (S. L. Schlagman, S. Hattman, and M. G. Marinus, J. Bacteriol. 165:896-900, 1986).
Descriptors: Escherichia **coli** --genetics--GE; *Genes, Structural, Viral; *Methyltransferases--genetics--GE; *Mutation; *Site-Specific DNA-Methyltransferase (Adenine-Specific); *T-Phages--genetics--GE; Cloning, Molecular; Escherichia **coli** --enzymology--EN; Phenotype; Plasmids; T-Phages --enzymology--EN
CAS Registry No.: 0 (Plasmids)
Enzyme No.: EC 2.1.1. (Methyltransferases); EC 2.1.1.- (Dam methyltransferase); EC 2.1.1.72 (Site-Specific DNA-Methyltransferase (Adenine-Specific))
Record Date Created: 19900605
Record Date Completed: 19900605

6/9/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08326251 PMID: 2510127
Single amino acid changes that alter the DNA **sequence specificity of the** DNA **-[N6-** adenine **]** methyltransferase **(Dam) of bacteriophage T4.**
Miner Z; Schlagman S L; Hattman S
Department of Biology, University of Rochester, NY 14627.

Nucleic acids research (ENGLAND) Oct 25 1989, 17 (20) p8149-57, ISSN 0305-1048 Journal Code: 0411011
Contract/Grant No.: GM29227; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Bacteriophage T4 codes for a DNA-[N6-adenine] methyltransferase (Dam) which recognizes primarily the sequence GATC in both cytosine- and hydroxymethylcytosine-containing DNA. Hypermethylating **mutants** , damh, exhibit a relaxation in sequence specificity, that is, they are readily able to methylate non-canonical sites. We have determined that the damh mutation produces a single amino acid change (Pro126 to Ser126) in a region of homology (III) shared by three DNA-adenine methyltransferases; viz, T4 Dam, Escherichia **coli** Dam, and the DpnII modification enzyme of Streptococcus pneumoniae. We also describe another **mutant** , damc, which methylates GATC in cytosine-containing DNA, but not in hydroxymethylcytosine-containing DNA. This mutation also alters a single amino acid (Phe127 to Val127). These results implicate homology region III as a domain involved in DNA sequence recognition. The effect of several different amino acids at residue 126 was examined by creating a polypeptide chain terminating codon at that position and comparing the methylation capability of partially purified enzymes produced in the presence of various suppressors. No enzyme activity is detected when phenylalanine, glutamic acid, or histidine is **inserted** at position 126. However, **insertion** of alanine, cysteine, or glycine at residue 126 produces enzymatic activity similar to Damh.

Tags: Support, U.S. Gov't, P.H.S.

Descriptors: DNA, Viral--genetics--GE; *Escherichia **coli** --genetics--GE; *Genes, Structural, Viral; *Mutation; *Proline; *Serine; *Site-Specific DNA-Methyltransferase (Adenine-Specific)--genetics--GE; *T-Phages--genetics --GE; Amino Acid Sequence; Base Sequence; Codon--genetics--GE; Escherichia **coli** --enzymology--EN; Kinetics; Molecular Sequence Data; Plasmids; Site-Specific DNA-Methyltransferase (Adenine-Specific) --isolation and purification--IP; Site-Specific DNA-Methyltransferase (Adenine-Specific) --metabolism--ME; T-Phages--enzymology--EN

CAS Registry No.: 0 (Codon); 0 (DNA, Viral); 0 (Plasmids); 147-85-3 (Proline); 56-45-1 (Serine)

Enzyme No.: EC 2.1.1.72 (Site-Specific DNA-Methyltransferase (Adenine-Specific))

Record Date Created: 19891204
Record Date Completed: 19891204

6/9/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08102612 PMID: 3072268

The DNA **[** adenine **-N6]** methyltransferase **(Dam) of bacteriophage T4.**

Schlagman S L; Miner Z; Feher Z; Hattman S
Department of Biology, University of Rochester, NY 14627.

Gene (NETHERLANDS) Dec 20 1988, 73 (2) p517-30, ISSN 0378-1119 Journal Code: 7706761
Contract/Grant No.: GM-29227; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

A functional bacteriophage T4 dam+ gene, which specifies a DNA [adenine-N6]methyltransferase (Dam), was cloned on a 1.8-kb HindIII fragment [Schlagman and Hattman, Gene 22 (1983) 139-156]. Sequence analysis [Macdonald and Mosig, EMBO J. 3 (1984) 2863-2871] revealed two overlapping in-phase open reading frames (ORFs). The 5' proximal ORF initiates translation at an AUG and encodes a 30-kDa polypeptide, whereas the

downstream ORF initiates translation at a GUG and encodes a 26-kDa polypeptide. Analysis of BAL 31 **deletions** in our original dam+ clone has verified that at least one of these overlapping ORFs, in fact, encodes T4 Dam. To investigate where T4 Dam translation is initiated, we have constructed plasmids in which a tac or lambda PL promoter is placed 5' to either the longer ORF or just the shorter ORF. Only clones which contain a promoter in front of the longer ORF produce active T4 Dam. This indicates that the 26-kDa polypeptide alone cannot be T4 Dam. Additional experiments suggest that only the 30-kDa polypeptide is required for enzyme activity and that the shorter ORF is not translated in plasmid-carrying cells. We also present evidence that T4 Dam is capable of methylating 5'-GATC-3', GATm5C, and GAThmC sequences; non-canonical sites (e.g., GACC) are also methylated, but much less efficiently.

Tags: Support, U.S. Gov't, P.H.S.

Descriptors: *Genes, Structural; *Genes, Viral; *Site-Specific DNA-Methyltransferase (Adenine-Specific)--genetics--GE; *T-Phages--genetics--GE; Cloning, Molecular; Escherichia **coli** --enzymology--EN; Escherichia **coli** --genetics--GE; Plasmids; Promoter Regions (Genetics); Recombinant Proteins--metabolism--ME; Saccharomyces cerevisiae--genetics--GE; Site-Specific DNA-Methyltransferase (Adenine-Specific)--metabolism--ME; T-Phages--enzymology--EN; Transformation, Genetic

CAS Registry No.: 0 (Plasmids); 0 (Recombinant Proteins)

Enzyme No.: EC 2.1.1.72 (Site-Specific DNA-Methyltransferase (Adenine-Specific))

Record Date Created: 19890605

Record Date Completed: 19890605

6/9/10 (Item 10 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

07870810 PMID: 2842672

A mutation in the DNA adenine methylase **gene (dam) of** Salmonella **typhimurium decreases susceptibility to 9-aminoacridine-induced frameshift mutagenesis.**

Ritchie L; Podger D M; Hall R M

CSIRO Division of Molecular Biology, North Ryde, NSW, Australia.

Mutation research (NETHERLANDS) Sep 1988, 194 (2) p131-41, ISSN 0027-5107 Journal Code: 0400763

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Subfile: INDEX MEDICUS

A **mutant** of **Salmonella** typhimurium with a reduced response to mutation induction by 9-aminoacridine (9AA) has been isolated. The mutation (dam-2) is located in the DNA adenine methylase gene. The dam-2 **mutant** strain exhibits a level of sensitivity to 2-aminopurine (2AP) intermediate between that of the dam+ and the DNA adenine methylation-deficit dam-1 strain, and 2AP sensitivity was reversed by introduction of a mutH mutation or of the plasmid pMQ148 (which carries a functional Escherichia **coli** dam+ gene). However, the dam-2 strain is not grossly defective in DNA adenine methylase activity. Whole cell DNA appears full methylated at -GATC- sites. The levels of 9AA required to induce equivalent levels of frameshift mutagenesis in the dam-2 strain were approximately 2-fold higher than for the dam+ strain. Introduction of pMQ148 dam+ reduced the level of 9AA required for induction of frameshift mutations 4-fold in the dam-2 strain and 2-fold in the dam+ strain. The dam-2 mutation had no effect on the levels of ICR191 required for induction of frameshift mutations, but introduction of pMQ148 reduced the ICR191-induced mutagenesis 2-fold. The dam+/pMQ148, dam-2/pMQ148 and dam-1/pMQ148 strains showed identical dose-response curves for both 9AA and ICR191. These results are consistent with a slightly reduced (dam-2) or increased (pMQ148) rate of methylation at the replication fork. The 2AP sensitivity of the dam-2 strain cannot be simply explained. Furthermore, addition of methionine to the assay medium reverses the 2AP sensitivity of the dam-2 strain, but has no effect on 9AA

mutagenesis.
Descriptors: Aminacrine--pharmacology--PD; *Aminoacridines--pharmacology --PD; *Genes, Bacterial; *Genes, Structural; *Methyltransferases--genetics --GE; *Mutation; * **Salmonella** typhimurium--genetics--GE; DNA **Transposable** Elements; Genotype; Microbial Sensitivity Tests; **Salmonella** typhimurium --drug effects--DE; **Salmonella** typhimurium--enzymology--EN; Site-Specific DNA-Methyltransferase (Adenine-Specific); Species Specificity
CAS Registry No.: 0 (Aminoacridines); 0 (DNA Transposable Elements); 90-45-9 (Aminacrine)
Enzyme No.: EC 2.1.1. (Methyltransferases); EC 2.1.1.72 (Site-Specific DNA-Methyltransferase (Adenine-Specific))
Record Date Created: 19881004
Record Date Completed: 19881004

6/9/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06951424 PMID: 3932821
Viability of Escherichia coli **K-12** DNA adenine methylase **(dam)** mutants **requires increased expression of specific genes in the SOS regulon.**
Peterson K R; Wertman K F; Mount D W; Marinus M G
Molecular & general genetics - MGG (GERMANY, WEST) 1985, 201 (1) p14-9, ISSN 0026-8925 Journal Code: 0125036
Contract/Grant No.: GM24496; GM; NIGMS; GM30330; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
We have examined the level of expression of the SOS regulon in cells lacking DNA adenine methylase activity (dam-). Mud (Ap, lac) fusions to several SOS operons (recA, lexA, uvrA, uvrB, uvrD, sulA, dinD and dinF) were found to express higher levels of beta-galactosidase in dam- strains than in isogenic dam+ strains. The attempted construction of dam- strains that were also **mutant** in one of several SOS genes indicated that the viability of methylase-deficient strains correlates with the inactivation of the SOS repressor (LexA protein). Consistent with this, the wild-type functions of two LexA-repressed genes (recA and ruv) appear to be required for dam- strain viability.
Tags: Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Descriptors: DNA Repair; *DNA, Bacterial--genetics--GE; *Escherichia **coli** --genetics--GE; *Genes, Bacterial; *Genes, Structural; *Methyltransferases--genetics--GE; *Mutation; Escherichia **coli** --enzymology--EN; Escherichia **coli** --growth and development--GD; Genotype ; Rec A Recombinases--genetics--GE; Site-Specific DNA-Methyltransferase (Adenine-Specific); Species Specificity; Transduction, Genetic; beta-Galactosidase--genetics--GE
CAS Registry No.: 0 (DNA, Bacterial)
Enzyme No.: EC 2.1.1. (Methyltransferases); EC 2.1.1.72 (Site-Specific DNA-Methyltransferase (Adenine-Specific)); EC 2.7.7.- (Rec A Recombinases) ; EC 3.2.1.23 (beta-Galactosidase)
Record Date Created: 19851218
Record Date Completed: 19851218

6/9/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06194633 PMID: 6307815
Molecular cloning of a functional dam+ gene coding for phage T4 DNA adenine methylase .
Schlagman S L; Hattman S
Gene (NETHERLANDS) May-Jun 1983, 22 (2-3) p139-56, ISSN 0378-1119

Journal Code: 7706761
Contract/Grant No.: GM-29227; GM; NIGMS
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

Phages T2 and T4 induce synthesis of a DNA-adenine methylase which is coded for by a phage gene, dam+. These enzymes methylate adenine residues in specific sequences which include G-A-T-C, the methylation site of the host Escherichia **coli** dam+ methylase. Methylation of G-A-T-C to G-m6A-T-C protects the site against cleavage by the MboI restriction nuclease. We have taken advantage of this property to enrich and screen for transformants which contain a cloned, functional T4 dam+ gene. These recombinant molecules consist of a 1.85-kb HindIII fragment **inserted** into the plasmid pBR322; both orientations of the fragment express the methylase gene, suggesting that transcription is from a T4 promoter. We have tested the 1.85-kb **insert** for sensitivity to a variety of restriction nucleases and have found single sites for EcoRI, BalI, XbaI, and at least two sites for BstNI (EcoRII). The relative positions of these restriction sites have also been determined. Physical mapping was carried out by Southern blot hybridization with 32P-labeled (nick-translated clone) probe. These experiments showed that the **insert** corresponds to a HindIII fragment located on the physical map of T4 between positions 16.2 and 18.1 kb from the T4rIIA-rIIB junction. E. **coli** dam- possesses several phenotypic differences from the wild-type dam+ parent, including an increased sensitivity to 2-aminopurine (2-AP). We found that T4 dam+ clones could relieve dam- cells of their increased sensitivity to 2-AP.

Tags: Support, U.S. Gov't, P.H.S.

Descriptors: *Cloning, Molecular; *DNA (Cytosine-5-)-Methyltransferase --genetics--GE; *Genes, Structural; *Genes, Viral; *Methyltransferases --genetics--GE; *T-Phages--genetics--GE; DNA Restriction Enzymes; Escherichia **coli** --enzymology--EN; Escherichia **coli** --genetics--GE; Nucleic Acid Hybridization; Site-Specific DNA-Methyltransferase (Adenine-Specific); T-Phages--enzymology--EN

Enzyme No.: EC 2.1.1. (Methyltransferases); EC 2.1.1.37 (DNA (Cytosine-5-)-Methyltransferase); EC 2.1.1.72 (Site-Specific DNA-Methyltransferase (Adenine-Specific)); EC 3.1.21 (DNA Restriction Enzymes)

Record Date Created: 19830920
Record Date Completed: 19830920

6/9/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06101268 PMID: 6300769

The isolation and characterization of the Escherichia coli DNA adenine methylase **(dam) gene.**

Brooks J E; Blumenthal R M; Gingeras T R

Nucleic acids research (ENGLAND) Feb 11 1983, 11 (3) p837-51, ISSN 0305-1048 Journal Code: 0411011
Contract/Grant No.: 5-R01-CA27275-02; CA; NCI; CA 09311-02; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS

The E. **coli** dam (DNA adenine methylase) enzyme is known to methylate the sequence GATC. A general method for cloning sequence-specific DNA methylase genes was used to isolate the dam gene on a 1.14 kb fragment, **inserted** in the plasmid vector pBR322. Subsequent restriction mapping and subcloning experiments established a set of approximate boundaries of the gene. The nucleotide sequence of the dam gene was determined, and analysis of that sequence revealed a unique open reading frame which corresponded in length to that necessary to code for a protein the size of dam. Amino acid

composition derived from this sequence corresponds closely to the amino acid composition of the purified dam protein. Enzymatic and DNA:DNA hybridization methods were used to investigate the possible presence of dam genes in a variety of prokaryotic organisms.
Tags: Support, U.S. Gov't, Non-P.H.S.; Support, U.S. Gov't, P.H.S.
Descriptors: Cloning, Molecular; *DNA (Cytosine-5-)-Methyltransferase --genetics--GE; *DNA, Bacterial--isolation and purification--IP; *Escherichia **coli** --enzymology--EN; *Genes, Bacterial; *Genes, Structural; *Methyltransferases--genetics--GE; Amino Acid Sequence; Base Sequence; DNA Restriction Enzymes; DNA, Bacterial--genetics--GE; Nucleic Acid Hybridization; Plasmids
Molecular Sequence Databank No.: GENBANK/J01600
CAS Registry No.: 0 (DNA, Bacterial); 0 (Plasmids)
Enzyme No.: EC 2.1.1. (Methyltransferases); EC 2.1.1.37 (DNA (Cytosine-5-)-Methyltransferase); EC 3.1.21 (DNA Restriction Enzymes)
Record Date Created: 19830527
Record Date Completed: 19830527

6/9/14 (Item 14 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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04988009 PMID: 370403
In vitro methylation of bacteriophage lambda DNA **by wild type (dam+) and** mutant **(damh) forms of the phage T2** DNA adenine methylase .
Brooks J E; Hattman S
Journal of molecular biology (ENGLAND) Dec 15 1978, 126 (3) p381-94, ISSN 0022-2836 Journal Code: 2985088R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Subfile: INDEX MEDICUS
Tags: Support, U.S. Gov't, P.H.S.
Descriptors: *Coliphages--genetics--GE; *DNA (Cytosine-5-)-Methyltransferase; *DNA, Viral; *Methyltransferases; Base Sequence; DNA (Cytosine-5-)-Methyltransferase--genetics--GE; Escherichia **coli** --genetics--GE; Methylation; Methyltransferases--genetics--GE; Mutation; Transfection
CAS Registry No.: 0 (DNA, Viral)
Enzyme No.: EC 2.1.1. (Methyltransferases); EC 2.1.1.37 (DNA (Cytosine-5-)-Methyltransferase)
Record Date Created: 19790516
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